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**Note:** Performing your original search, *antiplatelet solid tumor*, in PubMed will retrieve **4** citations.

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☐ 1: [Angiogenesis](#). 1999;3(1):53-60.



Links

**Inhibition of angiogenesis and tumor growth by murine 7E3, the parent antibody of c7E3 Fab (abciximab; ReoPro).**

**Varner JA, Nakada MT, Jordan RE, Collier BS.**

Department of Medicine, Cellular and Molecular Medicine East 3050,  
University of California, San Diego, La Jolla, CA 92093-0684, USA.  
jvarner@ucsd.edu

Angiogenesis plays an essential role in the growth and dissemination of solid tumor cancers. The expression of endothelial cell integrin alpha(v)beta3 has been shown to increase during vascular proliferation associated with human tumors. Selective antagonists of alpha(v)beta3 can block angiogenesis and tumor growth by inducing programmed cell death in proliferating endothelial cells. Monoclonal antibody 7E3, an antagonist of the human, but not murine, integrins alpha(v)beta3 and alphaIIb beta3 (GPIIb/IIIa), inhibits platelet aggregation. It is the parent antibody of a mouse/human chimeric antibody fragment approved for adjunctive therapy of patients undergoing percutaneous coronary interventions to prevent ischemic complications (c7E3Fab; abciximab; ReoPro). To evaluate the potential of 7E3 to inhibit human angiogenesis and tumor growth independent of its antiplatelet effects, we established integrin alpha(v)beta3-negative human melanoma tumors in full-thickness human skin grafted onto SCID mice. The resulting tumors induce a human angiogenic response as assessed by the immunoreactivity of vascular cells with monoclonal antibodies specific for human CD31. Administration of 7E3 prevented or significantly inhibited the growth of tumors, and this effect correlated with a significant reduction in the number of blood vessels supplying the tumors. These results support the previous findings that blockade of integrin alpha(v)beta3 inhibits angiogenesis and tumor growth and indicates that dual inhibitors of alpha(v)beta3 and alphaIIb beta3 are effective in blocking tumor growth and angiogenesis.

#### Related Links

Multiple roles for platelet GPIIb/IIIa and alphavbeta3 integrins in tumor growth, angiogenesis, and metastasis. [Cancer Res. 2002]

Abciximab (ReoPro, chimeric 7E3 Fab) demonstrates equivalent affinity and functional blockade of glycoprotein IIb/IIIa and alpha(v)beta3 integrins. [Circulation. 1998]

A peptidomimetic antagonist of the integrin alpha(v)beta3 inhibits Leydig cell tumor growth and the development of hypercalcemia of malignancy. [Cancer Res. 1998]

Potential future clinical applications for the GPIIb/IIIa antagonist, abciximab in thrombosis, vascular and oncological [Arterioscler Thromb Vasc Dis Res. 2000]

c7E3 Fab inhibits human tumor angiogenesis in a SCID mouse human skin xenograft model. [Angiogenesis. 2006]

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Apr 4 2007 12:47:27

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[Free Full Text](#)[Links](#)**Potential future clinical applications for the GPIIb/IIIa antagonist, abciximab in thrombosis, vascular and oncological indications.****Cohen SA, Trikha M, Mascelli MA.**

Cenrocor Inc. 200 Great Valley Parkway, Malvern, PA 19355, USA.,

Abciximab (ReoPro) is a mouse-human chimeric monoclonal antibody Fab fragment of the parent murine monoclonal antibody 7E3, and was the first of these agents approved for use as adjunct therapy for the prevention of cardiac ischemic complications in patients undergoing percutaneous coronary intervention (PCI). Abciximab binds with high avidity to both the non-activated and activated form of the GPIIb/IIIa receptor of platelets, the major adhesion receptor involved in aggregation. Additional cardiovascular indications for abciximab are unstable angina, carotid stenting, ischemic stroke and peripheral vascular diseases. Abciximab also interacts with two other integrin receptors; the  $\alpha$ v  $\beta$ 3 receptor, which is present in low numbers on platelets but in high density on activated endothelial and smooth muscle cells, and  $\alpha$ Mb  $\beta$ 2 integrin which is present on activated leukocytes. Cell types that express integrins GPIIb/IIIa and  $\alpha$ v  $\beta$ 3 such as platelets, endothelial and tumor cells have been implicated in angiogenesis, tumor growth and metastasis. Since abciximab interacts with high avidity to integrins GPIIb/IIIa and  $\alpha$ v  $\beta$ 3, it is reasonable to assume that it may possess anti-angiogenic properties in angiogenesis-related diseases, as well as anti-metastatic properties in case of disseminating tumors expressing the target integrin receptors.

PMID: 11033455 [PubMed - indexed for MEDLINE]

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Apr 4 2007 12:47:27

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1960	clopidogrel	US-PGPUB; USPAT	OR	ON	2007/04/20 10:29
L2	202556	((solid adj tumor) or oma or cancer or tumour or tumor or carcinoma or sarcoma)	US-PGPUB; USPAT	OR	ON	2007/04/20 10:31
L3	221735	((solid adj tumor) or ?oma or cancer or tumour or tumor or carcinoma or sarcoma)	US-PGPUB; USPAT	OR	ON	2007/04/20 10:31
L4	1268	l1 and l2	US-PGPUB; USPAT	OR	ON	2007/04/20 10:31
L5	1098	l4 and (platelet)	US-PGPUB; USPAT	OR	ON	2007/04/20 10:31
L6	204	l4 and (platelet)	USPAT	OR	ON	2007/04/20 10:56
L7	117	adp adj receptor	USPAT	OR	ON	2007/04/20 10:56
L8	356	adp adj receptor	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 11:55
L9	5157	l8 or (anti adj (platelet or clotting))	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 10:56
L10	944	l9 and (clopidogrel or plavix)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 11:31
L11	773	l10 and (solid or glioma or sarcoma or carcinoma)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 10:57
L12	95	l11 and (solid adj tumor)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 10:58
L13	2204	(clopidogrel or plavix)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 11:31
L14	276	(clopidogrel or plavix) and (lung near cancer)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 11:31
L15	103	l8 and (taxotere or radiosensitizing or radiation)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 11:59
L16	65	l15 and (cancer or neoplasm or tumor or neoplastic or sarcoma or carcinoma)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 11:59
L17	3187	taxotere and (taxotere or radiosensitizing or radiation)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 11:59

## EAST Search History

L18	3089	taxotere and (cancer or neoplasm or tumor or neoplastic or sarcoma or carcinoma)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 11:59
L19	63450	(radiation) and (cancer or neoplasm or tumor or neoplastic or sarcoma or carcinoma)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 11:59
L20	317165	(cancer or neoplasm or tumor or neoplastic or sarcoma or carcinoma)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 12:00
L21	10061	l19 and (solid adj tumor)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 12:01
L22	8453	l21 and (glioma or lung)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 12:01
L23	3559	l21 and (glioma and lung)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 12:01
L24	1024	l21 and (glioma and lung)	USPAT; DERWENT	OR	ON	2007/04/20 12:01
L25	1033	l23 and ((anti adj (thrombosis or thrombotic)) or adp)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/04/20 12:02
L26	252	l23 and ((anti adj (thrombosis or thrombotic)) or adp)	USPAT; DERWENT	OR	ON	2007/04/20 12:03
L27	157	l26 and (radiation adj therapy)	USPAT; DERWENT	OR	ON	2007/04/20 12:20
L28	2	"5707642".pn.	USPAT; DERWENT	OR	ON	2007/04/20 12:20
L29	2	"6211171".pn.	USPAT; DERWENT	OR	ON	2007/04/20 12:25
L30	2	"6384042".pn.	USPAT; DERWENT	OR	ON	2007/04/20 12:46
L31	25	trigger adj point adj therapy.	USPAT; DERWENT	OR	ON	2007/04/20 12:47
L32	2	l31 and fibromyalgia	USPAT; DERWENT	OR	ON	2007/04/20 12:47



=> s 12 <> or clopidogrel?

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FULL ESTIMATED COST	11.65	22.68

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S L3 OR CLOPIDOGREL?

          1546 CLOPIDOGREL?  
L5        1562 L4 OR CLOPIDOGREL?

=> s 15 and (solid tumor or cancer or neoplasm or carcinoma or sarcoma )

1071520 SOLID  
286987 SOLIDS  
1282589 SOLID  
          (SOLID OR SOLIDS)  
405122 TUMOR  
157223 TUMORS  
454786 TUMOR  
          (TUMOR OR TUMORS)  
12883 SOLID TUMOR  
          (SOLID(W) TUMOR)  
312986 CANCER  
45962 CANCERS  
324782 CANCER  
          (CANCER OR CANCERS)  
443852 NEOPLASM  
36419 NEOPLASMS  
460769 NEOPLASM  
          (NEOPLASM OR NEOPLASMS)  
158653 CARCINOMA  
32121 CARCINOMAS  
164 CARCINOMATA

166525 CARCINOMA  
(CARCINOMA OR CARCINOMAS OR CARCINOMATA)  
39008 SARCOMA  
4364 SARCOMAS  
102 SARCOMATA  
40678 SARCOMA

(SARCOMA OR SARCOMAS OR SARCOMATA)

L6 67 L5 AND (SOLID TUMOR OR CANCER OR NEOPLASM OR CARCINOMA OR SARCOMA )

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22823143 PD <=2002  
(PD<=20029999)

L7 16 L6 AND PD <=2002

=> focus  
PROCESSING COMPLETED FOR L7  
L8 16 FOCUS L7 1-

=> d ibib abs hitstr 1-16

L8 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:927185 CAPLUS

DOCUMENT NUMBER: 138:24716

TITLE: Preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents

INVENTOR(S): Cheng, Peter T.; Zhang, Hao; Hariharan, Narayanan

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 169 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

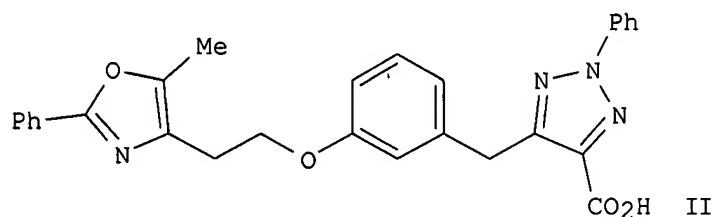
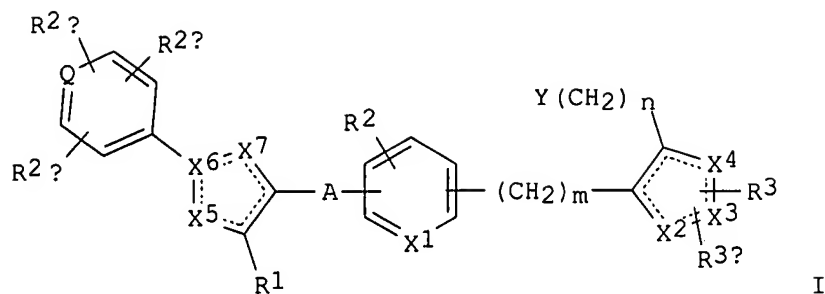
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

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WO 2002096358	A3	20030327		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2449160	A1	20021205	CA 2002-2449160	20020523 <--
EP 1390363	A2	20040225	EP 2002-729306	20020523
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TR 200400650	T3	20040621	TR 2004-650	20020523
HU 200401504	A2	20041129	HU 2004-1504	20020523
JP 2004536070	T	20041202	JP 2002-592871	20020523
TW 235061	B	20050701	TW 2002-91111100	20020524
PRIORITY APPLN. INFO.:			US 2001-294380P	20010530
			WO 2002-US16633	20020523

OTHER SOURCE(S): MARPAT 138:24716  
GI





AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH<sub>2</sub>)<sub>x</sub>, (CH<sub>2</sub>)<sub>x1</sub>, (CH<sub>2</sub>)<sub>x20</sub>(CH<sub>2</sub>)<sub>x3</sub>; x = 1-5; x<sub>1</sub> = 2-5; x<sub>2</sub>, x<sub>3</sub> = 0-5; ≥1 of x<sub>2</sub>, x<sub>3</sub> ≠ 0; X<sub>1</sub> = CH, N; X<sub>2</sub>, X<sub>3</sub>, X<sub>4</sub>, X<sub>5</sub>, X<sub>7</sub> = C, N, O, S; in each of X<sub>1</sub>-X<sub>7</sub>, C may include CH; R<sub>1</sub> = H, alkyl; R<sub>2</sub> = H, alkyl, alkoxy, halo, (substituted) amino; R<sub>2a</sub>, R<sub>2b</sub> and R<sub>2c</sub> = H, alkyl, alkoxy, halo, (substituted) amino; R<sub>3</sub>, R<sub>3a</sub> = H, alkyl, arylalkyl, aryloxy carbonyl, alkyloxy carbonyl, alkynyloxy carbonyl, alkenyloxy carbonyl, aryl carbonyl, alkyl carbonyl, aryl, heteroaryl, alkyl(halo)aryloxy carbonyl, alkoxy(halo)aryloxy carbonyl, cycloalkylaryloxy carbonyl, cycloalkyloxyaryloxy carbonyl, cycloheteroalkyl, heteroaryl carbonyl, heteroaryl heteroarylalkyl, alkyl carbonyl amino, aryl carbonyl amino, heteroaryl carbonyl amino, alkoxy carbonyl amino, aryloxy carbonyl amino, heteroaryl heteroaryl carbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryl oxy carbonyl, cycloheteroalkyloxy carbonyl, heteroarylalkyl, aminocarbonyl, substituted aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aryloxyarylalkyl, alkynyloxy carbonyl, haloalkoxyaryloxy carbonyl, alkoxy carbonyl aryloxy carbonyl, aryloxyaryloxy carbonyl, arylsulfinylaryl carbonyl, etc.; Y = CO<sub>2</sub>R<sub>4</sub>, 1-tetrazolyl, P(O)(OR<sub>4a</sub>)R<sub>5</sub>, P(O)(OR<sub>4a</sub>)<sub>2</sub>; R<sub>4</sub> = H, alkyl, prodrug ester; R<sub>4a</sub> = H, prodrug ester; R<sub>5</sub> = alkyl, aryl; with provisos], were prepared as simultaneous inhibitors of peroxisome proliferator activated receptor-γ (PPAR<sub>γ</sub>) and stimulators of peroxisome proliferator activated receptor-α (PPAR<sub>α</sub>). Thus, title compound (II) (prepared starting from Meldrum's acid 3-methoxyphenylacetyl chloride) bound to human PPAR<sub>α</sub> and to PPAR<sub>γ</sub> ligand binding domains with IC<sub>50</sub> = 69 nM.

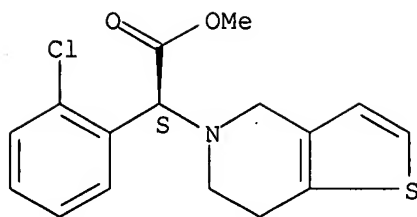
IT **113665-84-2, Clopidogrel**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(coadministration; preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents)

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α-(2-chlorophenyl)-6,7-dihydro-, methyl ester, (αS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L8 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:927184 CAPLUS

DOCUMENT NUMBER: 138:14048

TITLE: Preparation of oxazolylethoxyphenylprolines and related compounds as antidiabetic and antiobesity agents.

INVENTOR(S): Cheng, Peter T.; Jeon, Yoon; Wang, Wei

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 107 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096357	A2	20021205	WO 2002-US16628	20020523 <--
WO 2002096357	A3	20030925		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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US 7105556	B2	20060912		
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EP 1401433	A2	20040331	EP 2002-737192	20020523
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JP 2005506954	T	20050310	JP 2002-592870	20020523
HU 200600226	A2	20061128	HU 2006-226	20020523
US 2006189598	A1	20060824	US 2006-406799	20060419
PRIORITY APPLN. INFO.:			US 2001-294505P	P 20010530
			US 2002-153342	A3 20020522
			WO 2002-US16628	W 20020523

OTHER SOURCE(S): MARPAT 138:14048

GI



reductase inhibitors  
 INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S.  
 Ser. No. 875,155.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002094977	A1	20020718	US 2001-7407	20011204 <--
US 6627636	B2	20030930		
US 2002013334	A1	20020131	US 2001-875155	20010606 <--
PRIORITY APPLN. INFO.:			US 2000-211595P	P 20000615
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OTHER SOURCE(S):	MARPAT 137:109267			
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\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

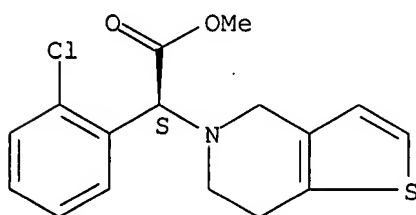
AB Title compds. I [X = O, S, SO, SO<sub>2</sub>, NR<sub>7</sub>; Z = HOCHCH<sub>2</sub>CH(OH)CH<sub>2</sub>CO<sub>2</sub>R<sub>3</sub>, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R<sub>1</sub>, R<sub>2</sub> = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R<sub>3</sub> = H, alkyl, metal ion; R<sub>4</sub> = H, halo, CF<sub>3</sub>, etc.; R<sub>7</sub> = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R<sub>9</sub>, R<sub>10</sub> = H, alkyl], were prepared as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, and atherosclerosis (no data). A multistep synthesis of II is reported.

IT 113665-84-2, Clopidogrel  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (coadministered agents; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L8 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:392331 CAPLUS

DOCUMENT NUMBER: 140:406798

TITLE: Preparation of benzoxepinopyridines as HMG-CoA

INVENTOR(S): reductase inhibitors  
 Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
 SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S.  
 Ser. No. 875,155, abandoned.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004092573	A1	20040513	US 2003-602752	20030624
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US 2002013334	A1	20020131	US 2001-875155	20010606 <--
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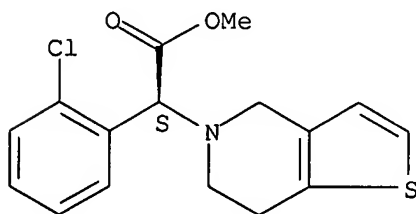
OTHER SOURCE(S): MARPAT 140:406798  
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\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I [X = O, S, SO, SO<sub>2</sub>, NR<sub>7</sub>; Z = HOCHCH<sub>2</sub>CH(OH)CH<sub>2</sub>CO<sub>2</sub>R<sub>3</sub>,  
 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R<sub>1</sub>, R<sub>2</sub> = alkyl, arylalkyl,  
 cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R<sub>3</sub>  
 = H, alkyl, metal ion; R<sub>4</sub> = H, halo, CF<sub>3</sub>, etc.; R<sub>7</sub> = H, alkyl, aryl,  
 alkanoyl, aroyl, alkoxycarbonyl, etc.; R<sub>9</sub>, R<sub>10</sub> = H, alkyl], were prepared as  
 HMG CoA reductase inhibitors active in inhibiting cholesterol  
 biosynthesis, modulating blood serum lipids such as lowering LDL  
 cholesterol and/or increasing HDL cholesterol, and treating  
 hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and  
 atherosclerosis (no data). A multistep synthesis of II is reported.

IT 113665-84-2, Clopidogrel  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (coadministered agents; preparation of benzoxepinopyridines as HMG-CoA  
 reductase inhibitors for treatment of hyperlipidemia,  
 hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other  
 disorders)  
 RN 113665-84-2 CAPLUS  
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-  
 dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

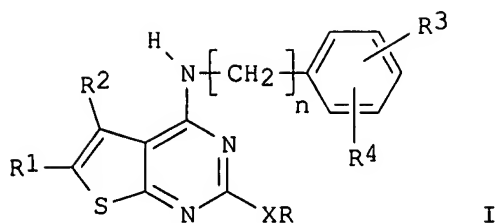


REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

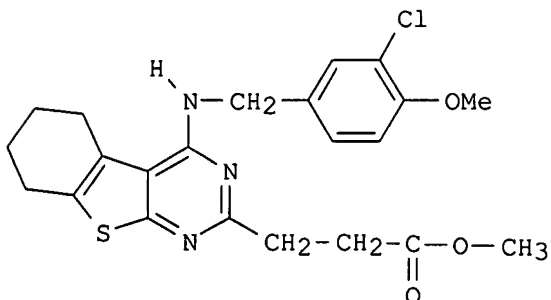
L8 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2002:487403 CAPLUS

DOCUMENT NUMBER: 137:47218  
 TITLE: Preparation of thieno[2,3-d]pyrimidine derivatives as phosphodiesterase V inhibitors and their pharmaceutical formulations containing antithrombotic, calcium antagonist, prostaglandin or prostaglandin derivative medicaments.  
 INVENTOR(S): Eggenweiler, Hans-Michael; Eiermann, Volker  
 PATENT ASSIGNEE(S): Merck Patent GmbH, Germany  
 SOURCE: PCT Int. Appl., 96 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002049650	A2	20020627	WO 2001-EP13915	20011128 <--
WO 2002049650	A3	20021031		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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DE 10063885	A1	20020711	DE 2000-10063885	20001221 <--
DE 10064992	A1	20020627	DE 2000-10064992	20001223 <--
CA 2431074	A1	20020627	CA 2001-2431074	20011128 <--
AU 200227957	A	20020701	AU 2002-27957	20011128 <--
EP 1347761	A2	20031001	EP 2001-989533	20011128
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR 2001016255	A	20031230	BR 2001-16255	20011128
HU 200303289	A2	20040128	HU 2003-3289	20011128
JP 2004516269	T	20040603	JP 2002-550990	20011128
NO 2003002772	A	20030618	NO 2003-2772	20030618
US 2004072846	A1	20040415	US 2003-451118	20030619
IN 2003KN00899	A	20050311	IN 2003-KN899	20030714
PRIORITY APPLN. INFO.:			DE 2000-10063223	A 20001219
			DE 2000-10063885	A 20001221
			DE 2000-10064992	A 20001223
			WO 2001-EP13915	W 20011128
OTHER SOURCE(S):	CASREACT 137:47218; MARPAT 137:47218			
GI				



I



II

AB This invention discloses the preparation of title compds. I and their pharmaceutically acceptable salts and solvates [wherein: R1, R2 independently = H, A, halogen, with the proviso that one of R1 or R2 always  $\neq$  H; or R1R2 = C3-5 alkylene; R3, R4 = H, A, OA, OH, halogen; or R3R4 = C3-5 alkylene, OCH2CH2, OCH2O, OCH2CH2O; X = C1-10 linear or branched alkyl with 1-2 optional CH:CH in lieu of CH2, C6H4(CH2)m, cycloalkylalkyl; R = CO2H, CO2A, CONH2, CONHA, CONA2, CN; A = alkyl; m = 1 or 2; n = 0-3]. For example, condensation of 4-chloro-5,6,7,8-tetrahydro[1]benzothieno[2,3-d]pyrimidine-2-propanoic acid Me ester and 3-chloro-4-methoxybenzylamine provided claimed thieno[2,3-d]pyrimidine-2-propanoate II as an oil. Pharmaceutical formulations containing I (as phosphodiesterase V inhibitors) in combination with an antithrombotic, calcium antagonist, prostaglandin or prostaglandin derivative are claimed for the treatment of angina, high blood pressure, pulmonary hypertension, congestive heart failure, chronic obstructive pulmonary disease (COPD), pulmonary heart disease, right ventricular failure, arteriosclerosis, permeability conditions of reduced cardiovascular patency, peripheral vascular illnesses, cerebral apoplexy, bronchitis, allergic asthma, chronic asthma, allergic rhinitis, glaucoma, irritable bowel syndrome, tumors, kidney failure, cirrhosis of the liver and for treating female sexual dysfunction (no data provided).

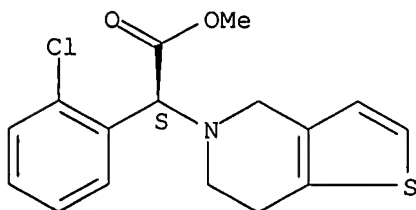
IT 113665-84-2, Clopidogrel

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical formulations with; preparation of benzothieno[2,3-d]pyrimidine derivs. for use in pharmaceutical formulations with antithrombotic, calcium antagonist, prostaglandin or prostaglandin derivative medicaments)

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L8 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:487402 CAPLUS

DOCUMENT NUMBER: 137:47217

TITLE: Preparation of benzothieno[2,3-d]pyrimidine derivatives as phosphodiesterase V inhibitors and their pharmaceutical formulations containing antithrombotic, calcium antagonist, prostaglandin or prostaglandin derivative medicaments.

INVENTOR(S): Eggenweiler, Hans-Michael; Eiermann, Volker

PATENT ASSIGNEE(S): Merck Patent Gmbh, Germany

SOURCE: PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

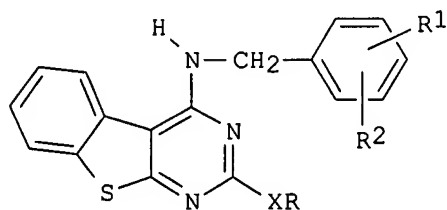
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

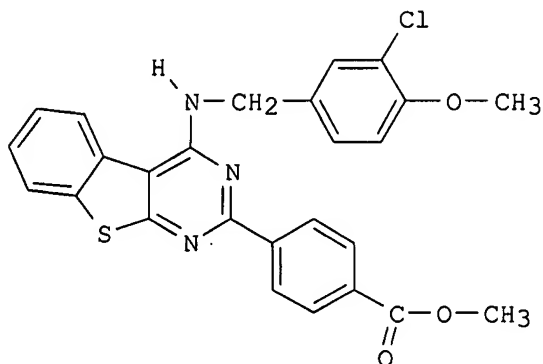
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002049649	A2	20020627	WO 2001-EP13913	20011128 <--
WO 2002049649	A3	20021121		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10063221	A1	20020620	DE 2000-10063221	20001219 <--
DE 10063884	A1	20020627	DE 2000-10063884	20001221 <--
DE 10064991	A1	20020627	DE 2000-10064991	20001223 <--
CA 2431147	A1	20020627	CA 2001-2431147	20011128 <--
AU 200226362	A	20020701	AU 2002-26362	20011128 <--
EP 1347762	A2	20031001	EP 2001-995677	20011128
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR 2001016247	A	20031104	BR 2001-16247	20011128
JP 2004516268	T	20040603	JP 2002-550989	20011128
NO 2003002771	A	20030618	NO 2003-2771	20030618
US 2004058940	A1	20040325	US 2003-451025	20030619
IN 2003KN00898	A	20050311	IN 2003-KN898	20030714
PRIORITY APPLN. INFO.:			DE 2000-10063221	A 20001219
			DE 2000-10063884	A 20001221
			DE 2000-10064991	A 20001223
			WO 2001-EP13913	W 20011128
OTHER SOURCE(S):	CASREACT 137:47217; MARPAT 137:47217			
GI				





I



II

AB This invention discloses the preparation of title compds. I and their pharmaceutically acceptable salts and solvates [wherein: R1, R2 = H, A, OA, OH, halogen; or R1R2 = C3-5 alkylene, OCH2CH2, CH2OCH2, OCH2O, OCH2CH2O; X = Ph, benzyl, cycloalkyl, cycloalkylalkyl, C1-10 linear or branched alkyl with 1-2 optional CH:CH in lieu of CH2; A = alkyl; R = CO2H, CO2A, CONH2, CONHA, CONA2, CN]. For example, condensation of 4-(4-chloro[1]benzothieno[2,3-d]pyrimidin-2-yl)benzoic acid Me ester and 3-chloro-4-methoxybenzylamine provided claimed [1]benzothieno[2,3-d]pyrimidin-2-ylbenzoate II (mp. 203-204°). Pharmaceutical formulations containing I (as phosphodiesterase V inhibitors) in combination with an antithrombotic, calcium antagonist, prostaglandin or prostaglandin derivative are claimed for the treatment of angina, high blood pressure, pulmonary hypertension, congestive heart failure, chronic obstructive pulmonary disease (COPD), pulmonary heart disease, right ventricular failure, arteriosclerosis, permeability conditions of reduced cardiovascular patency, peripheral vascular illnesses, cerebral apoplexy, bronchitis, allergic asthma, chronic asthma, allergic rhinitis, glaucoma, irritable bowel syndrome, tumors, kidney failure, cirrhosis of the liver and for treating female sexual dysfunction (no data provided).

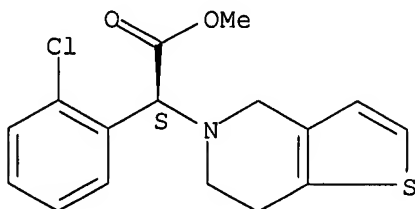
IT **113665-84-2, Clopidogrel**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical formulations with; preparation of benzothieno[2,3-d]pyrimidine derivs. for use in pharmaceutical formulations with antithrombotic, calcium antagonist, prostaglandin or prostaglandin derivative medicaments)

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L8 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:487404 CAPLUS

DOCUMENT NUMBER: 137:47219

TITLE: Preparation of pyrazolo[4,3-d]pyrimidine derivatives as phosphodiesterase V inhibitors and their pharmaceutical formulations containing antithrombotic, calcium antagonist, prostaglandin or prostaglandin derivative medicaments.

INVENTOR(S): Eggenweiler, Hans-Michael; Eiermann, Volker

PATENT ASSIGNEE(S): Merck Patent Gmbh, Germany

SOURCE: PCT Int. Appl., 94 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

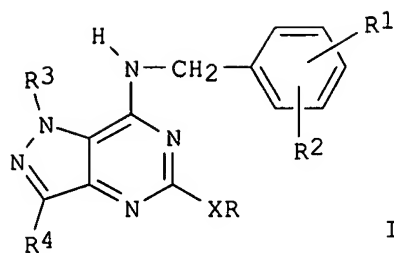
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

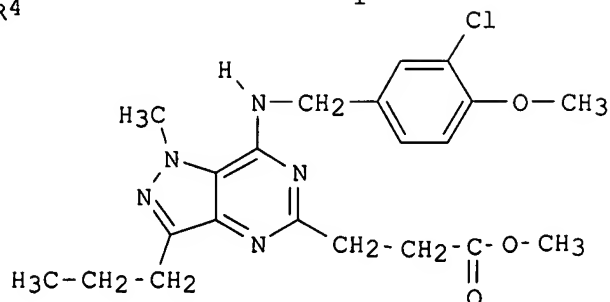
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002049651	A1	20020627	WO 2001-EP13916	20011128 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10063224	A1	20020620	DE 2000-10063224	20001219 <--
DE 10063882	A1	20020711	DE 2000-10063882	20001221 <--
DE 10064993	A1	20020704	DE 2000-10064993	20001223 <--
CA 2431077	A1	20020627	CA 2001-2431077	20011128 <--
AU 200229573	A	20020701	AU 2002-29573	20011128 <--
EP 1343506	A1	20030917	EP 2001-990452	20011128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001015995	A	20040113	BR 2001-15995	20011128
HU 200303315	A2	20040128	HU 2003-3315	20011128
JP 2004516270	T	20040603	JP 2002-550991	20011128
NO 2003002773	A	20030618	NO 2003-2773	20030618
US 2004063730	A1	20040401	US 2003-451105	20030619
IN 2003KN00905	A	20050311	IN 2003-KN905	20030715
PRIORITY APPLN. INFO.:			DE 2000-10063224	A 20001219
			DE 2000-10063882	A 20001221
			DE 2000-10064993	A 20001223
			WO 2001-EP13916	W 20011128

OTHER SOURCE(S): MARPAT 137:47219

GI



I



II

AB This invention discloses the preparation of title compds. I and their pharmaceutically acceptable salts and solvates [wherein: R1, R2 independently = H, A, OH, OA, halogen; or R1R2 = C3-5 alkylene, OCH2CH2, CH2OCH2, OCH2O, OCH2CH2O; R3, R4 independently = H, A; X = cycloalkyl, cycloalkylalkyl, Ph, benzyl, C1-10 linear or branched alkyl with 1-2 optional CH:CH in lieu of CH2, or optionally interrupted by O, S, or SO; R = CO2H, CO2A, CONH2, CONHA, CONA2, CN; A = alkyl]. For example, condensation of 3-[7-chloro-1-methyl-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl]propionic acid Me ester and 3-chloro-4-methoxybenzylamine provided claimed pyrazolo[4,3-d]pyrimidin-5-ylpropanoate II as an oil. Pharmaceutical formulations containing I (as phosphodiesterase V inhibitors) in combination with an antithrombotic, calcium antagonist, prostaglandin or prostaglandin derivative medicament are claimed for the treatment of angina, hypertension, pulmonary hypertension, congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), cor pulmonale, right ventricular failure, atherosclerosis, conditions of reduced patency of the heart vessels, peripheral vascular diseases, cerebrovascular accident, bronchitis, allergic asthma, chronic asthma, allergic rhinitis, glaucoma, irritable bowel syndrome, tumors, kidney failure, cirrhosis of the liver, and female sexual dysfunctions (no data provided).

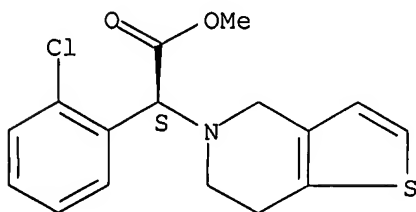
IT 113665-84-2, Clopidogrel

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical formulations with; preparation of benzothieno[2,3-d]pyrimidine derivs. for use in pharmaceutical formulations with antithrombotic, calcium antagonist, prostaglandin or prostaglandin derivative medicaments)

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2007:151052 CAPLUS  
DOCUMENT NUMBER: 146:244343  
TITLE: Peptides and peptide mimetics to treat pathologies characterized by an inflammatory response  
INVENTOR(S): Fogelman, Alan M.; Navab, Mohamad  
PATENT ASSIGNEE(S): The Regents of the University of California, USA  
SOURCE: U.S. Pat. Appl. Publ., 313pp., Cont.-in-part of U.S. Ser. No. 423,830.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 9  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007032430	A1	20070208	US 2006-407390	20060418
US 6664230	B1	20031216	US 2000-645454	20000824
US 2003045460	A1	20030306	US 2001-896841	20010629
US 6933279	B2	20050823		
CN 1375299	A	20021023	CN 2001-103876	20010823 <--
CN 1739787	A	20060301	CN 2005-10103876	20010823
CN 1911439	A	20070214	CN 2006-10100670	20010823
CN 1931358	A	20070321	CN 2006-10100667	20010823
CN 1931359	A	20070321	CN 2006-10100669	20010823
CN 1943781	A	20070411	CN 2006-10100668	20010823
US 2003171277	A1	20030911	US 2002-187215	20020628
US 7144862	B2	20061205		
US 2003229015	A1	20031211	US 2002-273386	20021016
US 7166578	B2	20070123		
US 2004266671	A1	20041230	US 2003-423830	20030425
US 7199102	B2	20070403		
JP 2006056899	A	20060302	JP 2005-304531	20051019
JP 2006312650	A	20061116	JP 2006-220831	20060814

PRIORITY APPLN. INFO.:

US 2000-645454	A2	20000824
US 2001-896841	A2	20010629
US 2002-187215	A2	20020628
US 2002-273386	A2	20021016
US 2003-423830	A2	20030425
US 2005-676431P	P	20050429
US 2005-697495P	P	20050707
CN 2001-103876	A3	20010823
CN 2001-817280	A3	20010823
CN 2005-10103876	A3	20010823
JP 2002-520844	A3	20010823
WO 2001-US26497	A2	20010823
JP 2005-304531	A3	20051019

OTHER SOURCE(S): MARPAT 146:244343

AB The invention provides novel active agents (e.g. peptides, small organic mols., amino acid pairs, etc.) that ameliorate one or more symptoms of atherosclerosis and/or other pathologies characterized by an inflammatory response. In certain embodiments, the peptides resemble a G\* amphipathic helix of apolipoprotein J. The agents are highly stable and readily administered via an oral route. Peptide preparation is included.

IT 113665-84-2, Clopidogrel

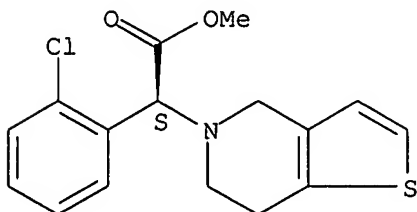
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptidic compds. to treat diseases characterized by inflammatory response)

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L8 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:462399 CAPLUS

DOCUMENT NUMBER: 137:47209

TITLE: Preparation of thieno[2,3-d]pyrimidine derivatives as phosphodiesterase V inhibitors and their pharmaceutical formulations containing antithrombotic medicaments.

INVENTOR(S): Eggenweiler, Hans-Michael; Eiermann, Volker

PATENT ASSIGNEE(S): Merck Patent GmbH, Germany

SOURCE: Ger. Offen., 30 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

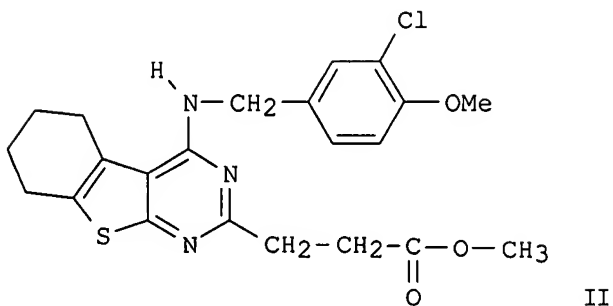
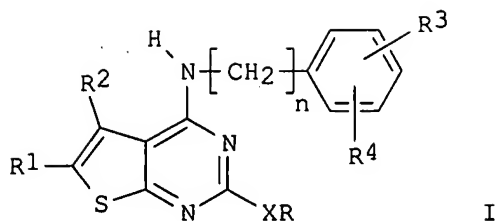
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10063223	A1	20020620	DE 2000-10063223	20001219 <--
CA 2431074	A1	20020627	CA 2001-2431074	20011128 <--
WO 2002049650	A2	20020627	WO 2001-EP13915	20011128 <--
WO 2002049650	A3	20021031		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 200227957	A	20020701	AU 2002-27957	20011128 <--
EP 1347761	A2	20031001	EP 2001-989533	20011128
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR 2001016255	A	20031230	BR 2001-16255	20011128
HU 200303289	A2	20040128	HU 2003-3289	20011128
JP 2004516269	T	20040603	JP 2002-550990	20011128
NO 2003002772	A	20030618	NO 2003-2772	20030618
US 2004072846	A1	20040415	US 2003-451118	20030619
IN 2003KN00899	A	20050311	IN 2003-KN899	20030714
ZA 2003005537	A	20041018	ZA 2003-5537	20030717
PRIORITY APPLN. INFO.:			DE 2000-10063223	A 20001219
			DE 2000-10063885	A 20001221
			DE 2000-10064992	A 20001223
			WO 2001-EP13915	W 20011128

OTHER SOURCE(S): CASREACT 137:47209; MARPAT 137:47209

GI



AB This invention discloses the preparation of title compds. I and their pharmaceutically acceptable salts and solvates [wherein: R1, R2 independently = H, A, halogen, with the proviso that one of R1 or R2 always  $\neq$  H; R1R2 = C3-5 alkylene; R3, R4 = H, A, OA, OH, halogen; R3R4 = C3-5 alkylene, OCH2CH2, OCH2O, OCH2CH2O; X = C1-10 linear or branched alkyl with 1-2 optional CH:CH in lieu of CH2, C6H4(CH2)m, cycloalkylalkyl; R = CO2H, CO2A, CONH2, CONHA, CONA2, CN; A = alkyl; m = 1 or 2; n = 0-3]. For example, condensation of 4-chloro-5,6,7,8-tetrahydro[1]benzothieno[2,3-d]pyrimidine-2-propanoic acid Me ester and 3-chloro-4-methoxybenzylamine provided claimed thieno[2,3-d]pyrimidine-2-propanoate II as an oil. Pharmaceutical formulations containing I (as phosphodiesterase V inhibitors) in combination with an antithrombotic medicament are claimed for the treatment of angina, (pulmonary) hypertension, congestive heart failure, arteriosclerosis, peripheral vascular diseases, stroke, bronchitis, allergic asthma, chronic asthma, allergic rhinitis, glaucoma, irritable bowel syndrome, tumors, kidney insufficiency, liver cirrhosis, and female sexual dysfunction (no data provided).

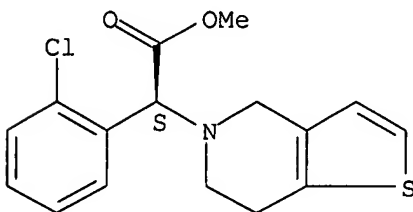
IT **113665-84-2, Clopidogrel**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical formulations with; preparation of thieno[2,3-d]pyrimidine derivs. for use in pharmaceutical formulations with antithrombotics)

RN 113665-84-2 CAPLUS

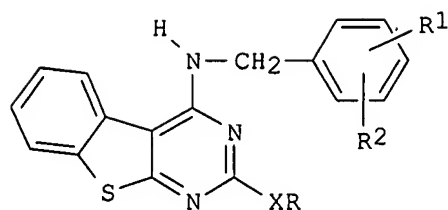
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

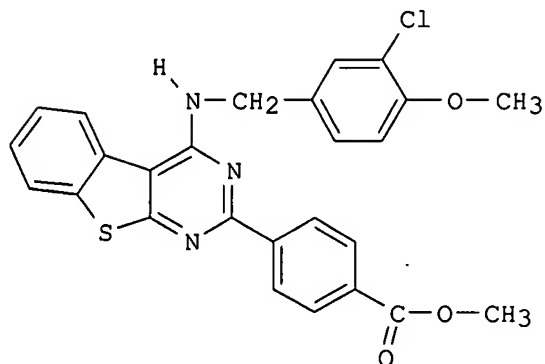


ACCESSION NUMBER: 2002:462398 CAPLUS  
 DOCUMENT NUMBER: 137:33315  
 TITLE: Preparation of [1]benzothieno[2,3-d]pyrimidine derivatives as phosphodiesterase V inhibitors and their pharmaceutical formulations containing antithrombotic medicaments.  
 INVENTOR(S): Eggenweiler, Hans-Michael; Eiermann, Volker  
 PATENT ASSIGNEE(S): Merck Patent GmbH, Germany  
 SOURCE: Ger. Offen., 26 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10063221	A1	20020620	DE 2000-10063221	20001219 <--
CA 2431147	A1	20020627	CA 2001-2431147	20011128 <--
WO 2002049649	A2	20020627	WO 2001-EP13913	20011128 <--
WO 2002049649	A3	20021121		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 200226362	A	20020701	AU 2002-26362	20011128 <--
EP 1347762	A2	20031001	EP 2001-995677	20011128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001016247	A	20031104	BR 2001-16247	20011128
JP 2004516268	T	20040603	JP 2002-550989	20011128
NO 2003002771	A	20030618	NO 2003-2771	20030618
US 2004058940	A1	20040325	US 2003-451025	20030619
IN 2003KN00898	A	20050311	IN 2003-KN898	20030714
ZA 2003005548	A	20041117	ZA 2003-5548	20030717
PRIORITY APPLN. INFO.:			DE 2000-10063221	A 20001219
			DE 2000-10063884	A 20001221
			DE 2000-10064991	A 20001223
			WO 2001-EP13913	W 20011128
OTHER SOURCE(S):			CASREACT 137:33315; MARPAT 137:33315	
GI				



I



II

AB This invention discloses the preparation of title compds. I and their pharmaceutically acceptable salts and solvates [wherein: R1, R2 = H, A, OA, OH, halogen; R1R2 = C3-5 alkylene, OCH2CH2, CH2OCH2, OCH2O, OCH2CH2O; X = Ph, benzyl, cycloalkyl, cycloalkylalkyl, C1-10 linear or branched alkyl with 1-2 optional CH:CH in lieu of CH2; A = alkyl; R = CO2H, CO2A, CONH2, CONHA, CONA2, CN]. For example, condensation of 4-(4-chloro[1]benzothieno[2,3-d]pyrimidin-2-yl)benzoic acid Me ester and 3-chloro-4-methoxybenzylamine provided claimed [1]benzothieno[2,3-d]pyrimidin-2-ylbenzoate II (mp. 203-204°). Pharmaceutical formulations containing I (as phosphodiesterase V inhibitors) in combination with an antithrombotic medicament are claimed for the treatment of angina, (pulmonary) hypertension, congestive heart failure, arteriosclerosis, peripheral vascular diseases, stroke, bronchitis, allergic asthma, chronic asthma, allergic rhinitis, glaucoma, irritable bowel syndrome, tumor, kidney insufficiency, liver cirrhosis, and female sexual dysfunction (no data provided).

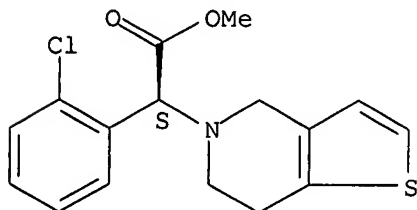
IT 113665-84-2, Clopidogrel

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical formulations with; preparation of [1]benzothieno[2,3-d]pyrimidine derivs. for use in pharmaceutical formulations with antithrombotics)

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

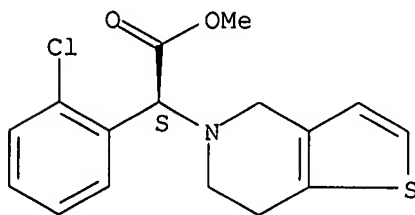




DOCUMENT NUMBER: 137:304829  
 TITLE: Enantiomers of N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-4-(2-oxazolyl)[1,1'-biphenyl]-2-yl]methyl]-N,3,3-trimethylbutanamide  
 INVENTOR(S): Hughes, David E.; Seidenberg, Beth C.  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
 SOURCE: PCT Int. Appl., 24 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083130	A1	20021024	WO 2002-US11992	20020412 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002254631	A1	20021028	AU 2002-254631	20020412 <--
US 2003040534	A1	20030227	US 2002-121520	20020412
PRIORITY APPLN. INFO.:			US 2001-284080P	P 20010416
			WO 2002-US11992	W 20020412
AB Endothelin antagonist N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-4-(2-oxazolyl)[1,1'-biphenyl]-2-yl]methyl]-N,3,3-trimethylbutanamide surprisingly exists as separable enantiomeric atropisomers. The (+)-dextrorotatory atropisomer demonstrates remarkably higher potency than either the (-)-levorotatory atropisomer or the racemate. The (+)-dextrorotatory atropisomer is suitable for treatment of endothelin-related disorders, such as hypertension, renal diseases, atherosclerosis, restenosis, congestive heart failure, diabetic nephropathy, cancer, asthma, etc., alone or in combination with, e.g., angiotensin, renin, or ACE inhibitors, diuretics, cardiac glycosides, antiplatelet agents, etc.				
IT 113665-84-2, Clopidogrel				
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combination with; therapeutic uses of enantiomers of biphenyl isoxazole sulfonamide derivative as endothelin antagonists)				
RN 113665-84-2 CAPLUS				
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)				

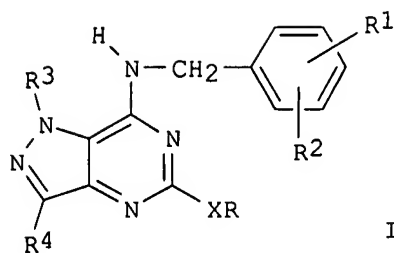
Absolute stereochemistry. Rotation (+).



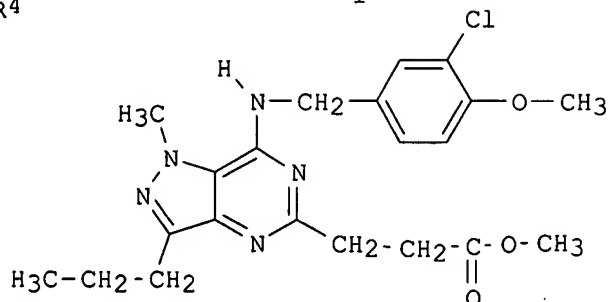
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 2002:462400 CAPLUS  
 DOCUMENT NUMBER: 137:47210  
 TITLE: Preparation of pyrazolo[4,3-d]pyrimidine derivatives  
 as phosphodiesterase V inhibitors and their  
 pharmaceutical formulations containing antithrombotic  
 medicaments.  
 INVENTOR(S): Eggenweiler, Hans-Michael; Eiermann, Volker  
 PATENT ASSIGNEE(S): Merck Patent GmbH, Germany  
 SOURCE: Ger. Offen., 28 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10063224	A1	20020620	DE 2000-10063224	20001219 <--
CA 2431077	A1	20020627	CA 2001-2431077	20011128 <--
WO 2002049651	A1	20020627	WO 2001-EP13916	20011128 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 200229573	A	20020701	AU 2002-29573	20011128 <--
EP 1343506	A1	20030917	EP 2001-990452	20011128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001015995	A	20040113	BR 2001-15995	20011128
HU 200303315	A2	20040128	HU 2003-3315	20011128
JP 2004516270	T	20040603	JP 2002-550991	20011128
NO 2003002773	A	20030618	NO 2003-2773	20030618
US 2004063730	A1	20040401	US 2003-451105	20030619
IN 2003KN00905	A	20050311	IN 2003-KN905	20030715
ZA 2003005542	A	20041117	ZA 2003-5542	20030717
PRIORITY APPLN. INFO.:				
			DE 2000-10063224	A 20001219
			DE 2000-10063882	A 20001221
			DE 2000-10064993	A 20001223
			WO 2001-EP13916	W 20011128
OTHER SOURCE(S): CASREACT 137:47210; MARPAT 137:47210				
GI				



I



II

AB This invention discloses the preparation of title compds. I and their pharmaceutically acceptable salts and solvates [wherein: R1, R2 independently = H, A, OH, OA, halogen; R1R2 = C3-5 alkylene, OCH2CH2, CH2OCH2, OCH2O, OCH2CH2O; R3, R4 independently = H, A; X = cycloalkyl, cycloalkylalkyl, Ph, benzyl, C1-10 linear or branched alkyl with 1-2 optional CH:CH in lieu of CH2, or optionally interrupted by O, S, or SO; R = CO2H, CO2A, CONH2, CONHA, CONA2, CN; A = alkyl]. For example, condensation of 3-[7-chloro-1-methyl-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl]propionic acid Me ester and 3-chloro-4-methoxybenzylamine provided claimed pyrazolo[4,3-d]pyrimidin-5-ylpropanoate II as an oil. Pharmaceutical formulations containing I (as phosphodiesterase V inhibitors) in combination with an antithrombotic medicament are claimed for the treatment of angina, (pulmonary) hypertension, congestive heart failure, arteriosclerosis, peripheral vascular diseases, stroke, bronchitis, allergic asthma, chronic asthma, allergic rhinitis, glaucoma, irritable bowel syndrome, tumor, kidney insufficiency, liver cirrhosis, and female sexual dysfunction (no data provided).

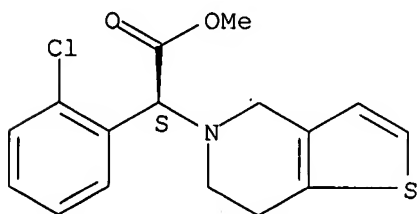
IT 113665-84-2, Clopidogrel

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical formulations with; preparation of pyrazolo[4,3-d]pyrimidine derivs. for use in pharmaceutical formulations with antithrombotics)

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L8 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:598215 CAPLUS

DOCUMENT NUMBER: 135:191313

TITLE: Polymorphisms in the human CYP2B6 gene and their use

INVENTOR(S): Zanger, Ulrich M.; Lang, Thomas  
 PATENT ASSIGNEE(S): Epidauros Biotechnologie A.-G., Germany  
 SOURCE: PCT Int. Appl., 83 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001059152	A2	20010816	WO 2001-EP1456	20010209 <--
WO 2001059152	A9	20020808		
WO 2001059152	A3	20021031		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1272663	A2	20030108	EP 2001-913809	20010209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004224313	A1	20041111	US 2002-958635	20020202
PRIORITY APPLN. INFO.:			EP 2000-102701	A 20000209
			WO 2001-EP1456	W 20010209

AB Described are general means and methods of diagnosing and treating the phenotypic spectrum as well as the overlapping clin. characteristics with several forms of inherited abnormal expression and/or function of the CYP2B6 genes encoding cytochrome P 450 2B6. In particular, polynucleotides of mol. variant CYP2B6 genes which, for example, are associated with insufficient metabolism and/or sensitivity of drugs, and vectors comprising such polynucleotides are provided. Furthermore, host cells comprising such polynucleotides or vectors and their use for the production of variant CYP2B6 proteins are described. In addition, variant

CYP2B6 proteins and antibodies specifically recognizing such proteins as well as transgenic non-human animals comprising the above-described polynucleotide or vectors are provided. Described are also methods for identifying and obtaining inhibitors for therapy of disorders related to the malfunction of the CYP2B6 gene as well as methods of diagnosing the status of such disorders. Pharmaceutical and diagnostic compns. useful for diagnosing and treating various diseases with drugs that are substrates, inhibitors or modulators of the CYP2B6 gene product are described as well.

IT 113665-84-2, Clopidogrel

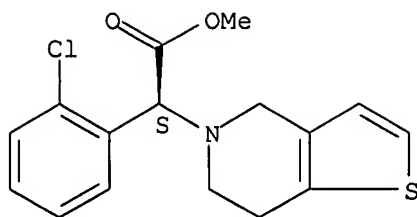
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(polymorphisms in the human CYP2B6 gene and their use in diagnostic and therapeutic applications, human cytochrome P 450 2B6 inhibitor)

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L8 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2005:77981 CAPLUS  
 DOCUMENT NUMBER: 142:162662  
 TITLE: Nanoparticulate glipizide compositions  
 INVENTOR(S): Bosch, H. William; Ryde, Niels P.  
 PATENT ASSIGNEE(S): Elan Pharma International Limited, USA  
 SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S.  
 Ser. No. 276,400.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 18  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005019412	A1	20050127	US 2003-701064	20031105
US 2002012675	A1	20020131	US 1999-337675	19990622 <--
WO 2001087264	A2	20011122	WO 2001-US15983	20010518 <--
WO 2001087264	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2004013613	A1	20040122	US 2003-276400	20030115
PRIORITY APPLN. INFO.:				
			US 1998-164351	B2 19981001
			US 1999-337675	A2 19990622
			WO 2001-US15983	W 20010518
			US 2003-276400	A2 20030115
			US 2000-572961	A 20000518

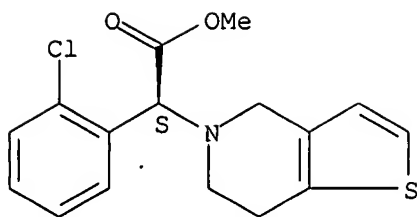
AB The present invention is directed to nanoparticulate compns. comprising glipizide. The glipizide particles of the composition preferably have an effective average particle size of <2  $\mu$ . Thus, a formulation contained spray-dried glipizide 5.33, mannitol 13.47, xylitol 40.53, citric acid 19.60, sodium bicarbonate 19.33, Asparatme 0.28, PEG-4000 0.93, and sodium stearyl fumarate 0.53%.

IT 113665-84-2, Clopidogrel  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (nanoparticulate glipizide compns.)

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L8 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2002:907166 CAPLUS  
 DOCUMENT NUMBER: 138:322  
 TITLE: Plasma glucosylceramide deficiency as risk factor for thrombosis and modulator of anticoagulant protein C  
 INVENTOR(S): Griffin, John H.; Deguchi, Hiroshi; Fernandez, Jose  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 32 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002177563	A1	20021128	US 2002-86943	20020228 <--
US 6756208	B2	20040629		
WO 2002102325	A2	20021227	WO 2002-US6340	20020228 <--
WO 2002102325	A3	20030912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1370570	A2	20031217	EP 2002-760992	20020228
EP 1370570	B1	20070124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 352309	T	20070215	AT 2002-760992	20020228
US 2004132688	A1	20040708	US 2003-739962	20031217
PRIORITY APPLN. INFO.:				
			US 2001-272103P	P 20010228
			US 2001-278045P	P 20010322
			US 2002-86943	A3 20020228
			WO 2002-US6340	W 20020228

AB The present invention has determined that exogenously added glucosylceramide (GlcCer) and other neutral glycolipids such as the homologous Glc-containing globotriaosylceramide (Gb3Cer), dose-dependently prolonged clotting times of normal plasma in the presence but not absence of APC:protein S, indicating GlcCer or Gb3Cer can enhance protein C pathway anticoagulant activity. In studies using purified proteins, inactivation of factor Va by APC:protein S was enhanced by GlcCer alone and by GlcCer, globotriaosylceramide, lactosylceramide, and galactosylceramide in multicomponent vesicles containing phosphatidylserine and phosphatidylcholine. Thus, the present invention provides neutral glycolipids such as GlcCer and Gb3Cer, as anticoagulant cofactors that contribute to the antithrombotic activity of the protein C pathway. The present invention has also determined that a deficiency of plasma GlcCer is a risk factor for

thrombosis. Methods are provided to determine individuals at risk for thrombosis, methods of treatment as well as methods of screening for antithrombotic factors from neutral glycolipids.

IT 113665-84-2, Clopidogrel

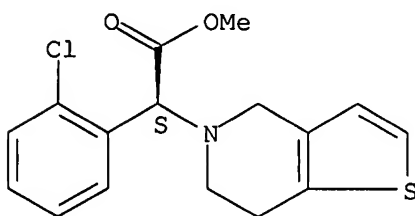
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(plasma glucosylceramide or other neutral glycolipid deficiency as risk factor for thrombosis and modulator of anticoagulant protein C when given in vesicle form in relation to combination with other agents)

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1178595 CAPLUS

DOCUMENT NUMBER: 146:740

TITLE: Peptides and peptide mimetics to treat pathologies characterized by an inflammatory response

INVENTOR(S): Fogelman, Alan M.; Navab, Mohamad

PATENT ASSIGNEE(S): The Regents of the University of California, USA

SOURCE: PCT Int. Appl., 143pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006118805	A2	20061109	WO 2006-US14839	20060418
WO 2006118805	A9	20070118		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

CN 1375299 A 20021023 CN 2001-103876 20010823 <--

PRIORITY APPLN. INFO.: US 2005-676431P P 20050429

US 2005-697495P P 20050707

AB This invention provides novel active agents (e.g. peptides, small organic mols., amino acid pairs, etc.) peptides that ameliorate one or more symptoms of atherosclerosis and/or other pathologies characterized by an

inflammatory response. In certain embodiment, the peptides resemble a G\* amphipathic helix of apolipoprotein J. The agents are highly stable and readily administered via an oral route. Synthetic procedures are described.

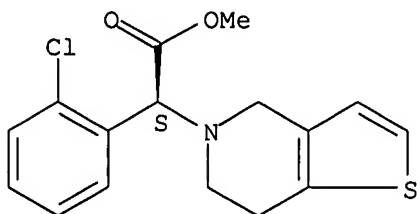
IT 113665-84-2, Clopidogrel

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(peptides and peptide mimetics for treatment of pathologies characterized by inflammatory response) .

RN 113665-84-2 CAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid,  $\alpha$ -(2-chlorophenyl)-6,7-dihydro-, methyl ester, ( $\alpha$ S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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L1 13 S CLOPIDOGREL

L2 1 S CLOPIDOGREL/CN

FILE 'CAPLUS' ENTERED AT 10:38:29 ON 20 APR 2007

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L5 1562 S L4 OR CLOPIDOGREL?

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13833 GLIOMA

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